

Amendments to the Claims:

This listing of claims will replace all prior versions and listings of claims in the application.

Listing of Claims:

1. (Currently Amended) ~~A novel~~ An isolated or synthesized polypeptide, wherein derived from

the polypeptide is a fragment of a Notch protein, wherein in a series of proteolytic events of the Notch protein,

N-terminal of the polypeptide is Site-2 cleavage site of the Notch protein that is positioned near a surface of cell membrane,

C-terminal of the polypeptide is Site-4 cleavage site of the Notch protein that is positioned on N-terminal side in a transmembrane domain of the Notch protein relative to Site-3 cleavage site, wherein the Site-3 cleavage site is positioned at either inside the cell membrane or in close proximity to the cell membrane inside the cell,

the polypeptide comprises at least a part of the transmembrane domain of the Notch protein,

the polypeptide is produced and released to an extracellular space when NICD (Notch intracellular cytoplasmic domain) translocates to a nucleus as a result of intramembranous endoproteolysis that occurs subsequent to extracellular proteolysis as a result of proteolysis at the Site-4 cleavage site that occurs simultaneously with, before, or after proteolysis at the Site-3 cleavage site, wherein the proteolysis at the Site-3 cleavage site occurs subsequent to proteolysis at the Site-2 cleavage site and translocates Notch intracellular cytoplasmic domain (NICD) to a nucleus of the cell, and

the Notch protein is a Notch protein that exists in an at least one organism selected from the group consisting of a human, a mouse, a rat, a rabbit, a goat, a swine, a bovine, a drosophila, and a nematode.

2. (Original) The polypeptide according to claim 1, which is released to the extracellular space in proportion to Notch signal transduction.

3. (Previously Presented) The polypeptide according to claim 1, wherein the release of the polypeptide to the extracellular space results from presenilin-dependent proteolysis.

4. (Cancelled)

5. (Cancelled)

6. (Withdrawn – currently amended) ~~A~~ An isolated or synthesized polypeptide comprising an amino acid sequence of at least one of SEQ ID NOS: 1 to 18.

7. (Withdrawn – currently amended) ~~A~~ An isolated or synthesized polypeptide comprising an amino acid sequence of at least one of SEQ ID NOS: 1 to 18 in which one or several of amino acids are deleted, substituted, or inserted, wherein the polypeptide is derived from a fragment of a Notch protein, and in a series of proteolytic events of the Notch protein,

N-terminal of the polypeptide is Site-2 cleavage site of the Notch protein that is positioned near a surface of cell membrane,

C-terminal of the polypeptide is Site-4 cleavage site of the Notch protein that is positioned on N-terminal side in a transmembrane domain of the Notch protein relative to Site-3 cleavage site, wherein the Site-3 cleavage site is positioned at either inside the cell membrane or in close proximity to the cell membrane inside the cell,

the polypeptide comprises at least a part of the transmembrane domain of the Notch protein,

the polypeptide is produced and released to an extracellular space when NICD translocates to a nucleus as a result of intramembranous endoproteolysis that occurs subsequent to extracellular proteolysis as a result of proteolysis at the Site-4 cleavage site that occurs simultaneously with, before, or after proteolysis at the Site-3 cleavage site,

wherein the proteolysis at the Site-3 cleavage site occurs subsequent to proteolysis at the Site-2 cleavage site and translocates (Notch intracellular cytoplasmic domain (NICD) to a nucleus of the cell, and

the Notch protein is a Notch protein that exists in an at least one organism selected from the group consisting of a human, a mouse, a rat, a rabbit, a goat, a swine, a bovine, a drosophila, and a nematode.

8. (Withdrawn) The polypeptide according to claim 7, which is released to the extracellular space in proportion to a Notch signal.
9. (Withdrawn) The polypeptide according to claim 7, wherein the release of the polypeptide to the extracellular space results from presenilin-dependent proteolysis.
10. (Withdrawn) A biomarker comprising the polypeptide according to claim 1.
11. (Withdrawn) The biomarker according to claim 10 for detecting at least one selected from the group consisting of Notch signal transduction, cell differentiation, tumor, apoptosis, and Alzheimer's disease.
12. (Withdrawn) An antibody that can recognize the polypeptide according to claim 1.
13. (Withdrawn – currently amended) The antibody according to claim 12, which is at least one of a monoclonal antibody ~~or~~ and a polyclonal antibody.
14. (Withdrawn) A reagent for detecting at least one selected from the group consisting of Notch signal transduction, cell differentiation, tumor, apoptosis, and Alzheimer's disease, which comprises the antibody according to claim 12.
15. (Withdrawn – currently amended) A gene encoding the polypeptide according to claim 1.

16. (Withdrawn) The gene according to claim 15, which is DNA or RNA.
17. (Withdrawn – currently amended) A vector comprising the gene according to claim 15.
18. (Withdrawn) A transformant transformed with the vector according to claim 17.
19. (New) The polypeptide according to claim 1, wherein an amino acid sequence of the polypeptide is at least one selected from the group consisting of SEQ ID NOS: 1 to 18.
20. (New) The polypeptide according to claim 1, wherein an amino acid sequence of the polypeptide is at least one selected from the group consisting of SEQ ID NOS: 1 to 18 in which one or several of amino acids are deleted, substituted, or inserted.
21. (New) The polypeptide according to claim 1, wherein the polypeptide comprises an amino acid sequence at least one selected from the group consisting of
an amino acid sequence consisting of the 1st residue to the 8th residue of SEQ ID NOS: 37 and 38, and
an amino acid sequence consisting of the 1st residue to the 6th residue of SEQ ID NOS: 39 to 44.